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Case Report

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Primary anorectal melanoma: a case of 5 year disease-free survival

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ABSTRACT

Anorectal melanoma is a rare cause of anorectal malignancies affecting mainly elderly people without significant gender differences, although there seems to be a white predominance. Diagnosis is often challenging, since symptoms are frequently nonspecific. Radical surgery is the mainstay of treatment, while adjuvant therapies are generally of limited value. Thus, prognosis is still grim, with a 5-year survival rate of less than 20%. We report the case of a 75-year-old white female presenting with mild anal pain and blood in stools. Diagnosed with an ulcerated melanoma of the perianal area, she eventually underwent an abdominoperineal resection and bilateral inguinal lymphadenectomy. To date, she is currently alive and disease-free. Given the lack of adequate international guidelines, we recommend defining a tailored treatment by thorough multidisciplinary discussion, as well as taking into account the patient personal preference.

Keywords: Anorectal, Bleeding, Melanoma, Surgery, Therapy

INTRODUCTION

Anorectal melanoma is a rare form of melanoma affecting the anus and/or rectum. It accounts for 0.25-1.25% of all anorectal malignancies and is the third most common site for melanoma, after the skin and eye.[1] Anorectal melanoma affects mainly people aged 50-80 years, with peak incidence in the sixth and seventh decades of life. There are no significant gender differences, whereas the Caucasian race seems to be more frequently affected than African American individuals.[1]

Diagnosis is often delayed, since symptoms are frequently nonspecific and easily mistaken for more benign conditions, such as hemorrhoids. Radical surgery is the mainstay of treatment, while the role of adjuvant chemotherapy, immune therapy and radiotherapy is yet to be established. Prognosis is therefore extremely poor with an average survival of 8-24 months and a 5-year survival rate of 10-15%.[1,2]

CASE REPORT

A 75-year-old Caucasian woman was seen in April 2011 with a two-month history of occasional rectal bleeding and moderate anal pain. Her medical history was remarkable for ischemic cardiomyopathy and obesity (body mass index 30 kg/m^2). On a more accurate anamnesis, she reported the removal of a blue nevus of the foot dorsum about ten years earlier. She denied any other significant personal and family history.

Considering the clinical findings, the patient underwent a colonoscopy with removal of three polyps with low-grade dysplasia. The endoscopy also revealed a blackish perianal lesion, fragile and easy to bleed, on which biopsies were taken (Figure 1). Histopathologic findings were consistent with a melanomatous lesion. On lab tests, S-100 protein was slightly positive. An accurate staging of the disease was also performed by means of ultrasound of the regional lymph nodes, chest radiography, and

whole-body PET-CT, with no evidence of distant metastases.

Figure 1: Primitive rectal melanoma discovered during colonoscopy.

After a thorough multidisciplinary team discussion (including surgeons, gastroenterologists, dermatologists and oncologists), a conservative approach was proposed and the patient underwent a trans-anal excision of the melanomatous lesion. Pathologic examination of the resected specimen confirmed the presence of a nodular, ulcerated, mucosal melanoma, with low mitotic index and Breslow index of 10 mm, invading the submucosa and muscle tunica of the rectum, with perilesional lympho-plasmacellular infiltration and no inflammatory intra-lesional infiltrates. Excision surgical margins were disease-free. The post-operative course was uneventful, albeit the patient briefly required medication for a wound dehiscence. Soon afterwards, she was started on adjuvant immunotherapy with interferon-gamma according to the Kirkwood protocol (IntronA 3 MU s.c. three times per week). Considering the good tolerance to the drug, the patient continued the immunotherapy for 18 months, until December 2012.

In September 2012, at 15 months from surgery, the patient presented at a follow-up examination complaining rectal bleeding. A colonoscopy was consequently performed and a local relapse of disease was found (Figure 2).

There was no evidence of metastatic disease on preoperative imaging and the patient underwent an abdominoperineal resection (Miles operation). She well tolerated the surgical procedure without any complications. Final histopathologic analysis showed a recurrent rectal melanoma, nodular and ulcerated, with free resection margins and metastatic deposit in one mesorectal lymph node out of 20 identified.

In July 2013, suspicious bilateral inguinal lymphadenopathy was noticed and an ultrasound-guided fine needle aspiration (FNA) was performed. Cytologic examination confirmed the suspect of bilaterally metastatic disease, while on thoraco-abdominal imaging no evidence of further secondary localizations was found. Thus, the patient underwent bilateral inguinal lymphadenectomy. To date, she is still alive and currently disease-free.

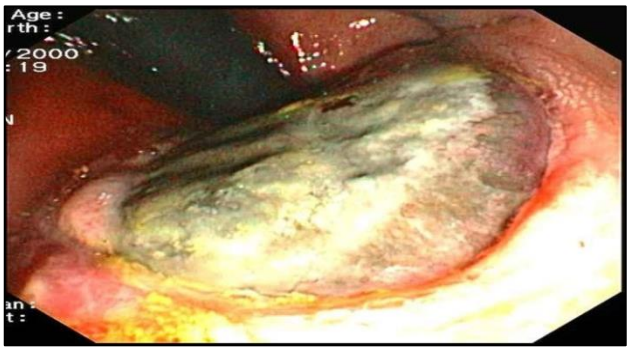

Figure 2: Recurrence of rectal melanoma diagnosed during follow-up colonoscopy.

DISCUSSION

Primary malignant melanoma of the anus and rectum is a rare form of melanoma associated with a poor prognosis. It represents 0.25-1.25% of all anorectal malignancies and it accounts for less than 1% of all melanomas, although it is the third most common location after cutaneous and ocular sites.[1,2] The incidence of primary anorectal melanoma is continuously increasing over time.[3] It arises from melanocytes, which are cells derived from the embryologic neural crest and reside primarily in the skin, but can also be found in the eyes and mucosal surfaces.

Anorectal melanoma was first reported by Moore in 1857.[4] The clinical and pathological features were first reported in 1963 by Morson and Volkstadt, who outlined eleven different types of "implant" of the lesion in the anal canal, relatively to its position with respect to the dentate line. Indeed, melanomatous lesions can affect the anal canal, the rectum, or both, with the majority occurring within 6 cm of the anal rim.[5,6]

The exact causes of anorectal melanoma are not established yet. Sunlight exposure, particularly UVB radiation, is a well-known risk factor for cutaneous melanoma, but to date it is still unclear what triggers the development of mucosal melanoma, and specifically anorectal melanoma. Interestingly, some authors have suggested a possible association with HIV and HHV-8 infection, but data are still controversial.[7-9]

Anorectal melanoma commonly affects the elderly in their sixth or seventh decade of life, with a 1.7 - fold higher prevalence in Caucasians than in African Americans.[1] Some authors report a possible female predominance, but most publications do not suggest significant gender differences and individual series are too small to draw definitive conclusions.[7-11]

Lesions are usually polypoid, often ulcerated and easy to bleed, with or without pigmentation.[12] Melanin pigment

within the malignant cells and junctional changes, e.g. the presence of atypical epidermoid cells or pleomorphic spindle cells adjacent to the focus of malignant tumor, help histologic diagnosis. Immunochemistry panels can also support the diagnosis. Indeed, melanoma antigens S-100, HMB-45, and vimentin are stained positively in 78%, 94%, and 100% of tumors respectively, while monoclonal antibodies to CEA can help to distinguish from a poorly differentiated epidermoid carcinoma.[11]

Diagnosis of anorectal melanoma is clinically challenging because symptoms are often nonspecific. Patients commonly present with rectal bleeding, anorectal pain or discomfort, change in bowel habits, and prolapsed tumor mass. If metastatic disease is present, weight loss, anemia, fatigue, groin swelling, or pelvic masses may be present as well.[11,13-16] Patients are often misdiagnosed with more common diseases, including hemorrhoids, polyp, adenocarcinoma, or rectal ulcer.[6] A timely diagnosis of anorectal melanoma is made even more difficult by the fact that up to 80% of lesions lack obvious pigmentation and up to 20% of tumors are even histologically amelanotic.[5,17]

Therefore, patients presenting with bleeding and/or anorectal pain should undergo a thorough examination of the colon and rectum, and biopsies of any suspicious lesion should be obtained. Rarely, anal melanoma can be identified during routing pathologic examination of a hemorrhoidectomy specimen.[18] Important staging tools include ultrasound of regional lymph nodes, CT scan of the abdomen and chest, and pelvic MRI scan. The best imaging exam to detect lymph node metastasis and distant metastasis is the PET-CT, which appeared to be superior to CT scan.[19]

Because of the delays in diagnosis and the aggressive nature of the disease, patients with anorectal melanoma frequently present with advanced disease. Common sites of metastasis are the regional lymph nodes, liver and lungs.[20] Average survival is of 8-24 months, with a 5-year survival rate of 10-15%.[21] Prognostic factors include the stage of the disease at the time of diagnosis and the tumor thickness.[22,23]

At present, surgery represents the mainstay of treatment, but the optimal approach is still controversial. Surgical intervention includes wide local excision (WLE) and abdomino-perineal resection (APR).[19,24] Several studies failed to demonstrate any survival advantage with either approach.[23,25-27] Chen et al. recommended surgery as the optimal treatment for local- and regional-stage anorectal melanoma, but not in case of distant metastasis.[3] Recently, some authors suggested the initial treatment of choice to be WLE, because more radical approaches did not show any survival advantage and conservative surgery also avoid the need for a permanent colostomy.[24] On the other side, local disease appears to be more effectively controlled with APR.[14,28,29] Likewise, current guidelines are not clear regarding sentinel lymph node biopsy. Although feasible and the preferred method of nodal staging for cutaneous melanoma, its role for staging of anal melanoma remains uncertain.[11,30-32]

In a recent paper by Ciarrocchi et al. was reported that metastasis to loco-regional lymph-nodes was an important prognostic factor, but lymphadenectomy did not improve survival.[33] In our patient the bilateral lymphadenectomy appeared to be curative, since she is still alive after more than three years from the surgical procedure.

As for adjuvant therapies, there are no standard approved regimens and strategies are mainly aimed at local control of the disease. Radiotherapy has been reported to improve local control after WLE and appears beneficial for sphincter preservation.[12,14,24,32] Patients with metastatic anorectal melanoma may benefit from combination chemotherapy. Many agents have been studied, including dacarbazine, vincristine, and interferon, but none has shown significant survival benefit for anorectal melanoma.[11]

CONCLUSION

Anorectal melanoma is a rare and aggressive malignancy affecting mainly elderly people. Early diagnosis and treatment are crucial, but symptoms are frequently aspecific and vague. Prognosis is generally poor, with distant metastases being a common and fatal development. Due to the rarity of the disease and lack of prospective randomized trials, the ideal multimodality therapy for anorectal melanoma is yet to be defined. Surgery is currently the mainstay of treatment and a more conservative approach should be preferred whenever technically feasible, in order to minimize patient morbidity and maximize quality of life. Inguinal lymphadenectomy should be reserved for clinically palpable disease, whereas the role of adjuvant therapies is still under debate.

As was the case of our patient, the treatment of choice at the beginning was defined by a more conservative surgical approach associated to systemic immunotherapy. A close follow-up subsequently allowed an early identification of the local relapse and a complete R0 surgical excision was completed.

According to our personal experience, given the lack of adequate international guidelines, we recommend defining a tailored treatment by thorough multidisciplinary discussion, which should include specialists in oncology, dermatology, pathology, and surgery, as well as taking into account the patient personal preference.

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